# Lead as a Cause of SIDS

The Harvard community has made this article openly available. Please share how this access benefits you. Your story matters.

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Published Version</td>
<td>doi:10.1056/NEJM198510103131511</td>
</tr>
<tr>
<td>Citable link</td>
<td><a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:34216536">http://nrs.harvard.edu/urn-3:HUL.InstRepos:34216536</a></td>
</tr>
<tr>
<td>Terms of Use</td>
<td>This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA">http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA</a></td>
</tr>
</tbody>
</table>
Previous attempts to demonstrate the presence of virus in circulating lymphocytes have been unrewarding. Measles virus antigens have been detected after stimulation with phytohemagglinulin in lymphocytes from a small number of patients with SSPE, and virus has been recovered from lymph-node biopsy specimens. These sporadic reports confirm the general view that lymphocytes become infected in the course of measles infection and a small number of these cells persist, although the type of cell affected and the nature of the viral imprint is not known. In vitro studies of human lymphocytes infected with measles virus have demonstrated both impaired killer-cell activity and impaired immunoglobulin synthesis. This occurs at a time when the lymphocytes appear normal and are not producing demonstrable measles-virus gene products.

If the majority of circulating lymphocytes contain viral genetic material similar to that present throughout the brain, then the challenge is to characterize better the type of lymphocyte involved and the chronology of that involvement. If these are T cells, as suggested, the important next question is whether they are a specific subpopulation or possibly clonally derived. It seems unlikely that this number of circulating lymphocytes would acquire viral RNA as a result of exposure to virus in the nervous system. The reverse may be true, in the sense that infected lymphocytes may transmit virus to the brain at the time of the initial viremia. If these lymphocytes can be shown to be derived from a single clone, the disease mechanism may be linked in some way to that selection process, as originally proposed by Burnet. The gradual increase in the numbers of lymphocytes containing RNA sequences may be a factor influencing the onset of disease. Alternatively, if most of the lymphocytes were infected during the initial viremia, a transient state of immune suppression may have resulted, allowing virus to reach the central nervous system unchallenged. One might then argue that the remaining uninfected lymphocytes become sensitized by exposure to these cells, and that this accounts for the variable expression of cell-mediated immunity found in these patients.

Obviously, there are many questions remaining, and the final chapter of the SSPE story may not be written for years. However, the opportunity is now presented to examine the role of the immune system in this disease in greater detail. In so doing, we should learn how lymphocytes are affected by the presence of viral RNA, and possibly what the processes are of viral entry into these cells and of abortive viral replication. How lymphocytes interact with brain tissue and the role they may have in disease progression and arrest are questions that may now be answerable. In this regard it is probably timely to reexamine the lymphocytes from patients with multiple sclerosis, using similar hybridization techniques. Numerous studies over the years have suggested differences in the levels of measles antibodies in these patients as compared with control groups. Admittedly, these differences have not been great, and virus has not been detected in brain tissue. However, in measles virus encephalitis there is convincing evidence of white-matter involvement, without virus replication in the nervous system. Obviously, the nervous system reacts in a number of ways to infection with this virus, and the dependent variable is presumably the host's ability to respond at the time of the initial infection.

Although our knowledge of SSPE remains incomplete, substantial progress has been made in recent years and at a time when clinicians have forgotten about the condition because few new cases are occurring, at least in countries with comprehensive measles-immunization programs. Nevertheless, a continued research effort to delineate the mechanism of this complex disease needs no defense, considering the relevance of what we may learn for a better understanding of both SSPE and other atypical viral infections of the human nervous system.

University of Tennessee Memphis, TN 38103

John F. Griffith, M.D.

REFERENCES


CORRESPONDENCE

LEAD AS A CAUSE OF SIDS

To the Editor: The sudden infant death syndrome (SIDS) is an enigmatic disease of unknown cause. Recent research suggests that a key to an understanding of its pathogenesis may be found by studying the survivors, or "near misses," of SIDS incidents.

From epidemiologic data, both environmental and social risk factors are known. The combination of risk indicators suggests that exposure to pollution may be important. Hopenbourn et al. found a correlation with air-pollution factors, including lead, and Erickson et al. demonstrated an increased tissue concentration of lead in children with SIDS, as compared with the level in children who had died from other causes.
Table 1. Summary Data on Three Children with an Episode of “Near-Miss” Sudden Infant Death.

<table>
<thead>
<tr>
<th>CASE NO.</th>
<th>AGE AT EPISODE</th>
<th>MONTH/TIME ACTIVITY</th>
<th>ACTION BY CARETAKER</th>
<th>DENTIN LEAD*</th>
<th>POSSIBLE SOURCE OF EXCESS LEAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11 days</td>
<td>March/11 p.m./sleep</td>
<td>Vigorous stimulation, contact with family doctor</td>
<td>26.9</td>
<td>Mother’s occupation (secretary in a printing house)</td>
</tr>
<tr>
<td>2</td>
<td>8 months</td>
<td>January/5 p.m./nap</td>
<td>Resuscitation by professional nurse, transfer to hospital</td>
<td>21.1</td>
<td>Heavily trafficked road (35,000 vehicles/day)</td>
</tr>
<tr>
<td>3</td>
<td>12 days</td>
<td>September/3 p.m./nap</td>
<td>Resuscitation by mother and ambulance personnel, transfer to hospital</td>
<td>43</td>
<td>Father’s occupation (welder)</td>
</tr>
</tbody>
</table>

*The geographic mean of circumpal lead in Aarhus children is 3.9 µg per gram. The limit used as "high" in the investigation was >18.7 µg per gram, accounting for 8 per cent of the distribution.

In 1983-1984 first-grade children in the municipality of Aarhus, Denmark, were screened for lead absorption by measurement of the lead concentration in the secondary dentin of shed deciduous teeth. The screened cohort of 1302 children constituted 54 per cent of the eligible population. Children with the upper 8 per cent of tooth lead concentrations were selected and matched with children with the lowest concentrations, according to parental social group, sex, and school district.

A pedestrian who was blind to the lead data interviewed the parents about morbidity in the children, the medical background, and the possible sources of lead.

From interviews with 101 families of children with high levels of lead and 99 families of those with low levels, three cases of "near-miss" SIDS were found; they all belonged to the high-level group (Table 1). Assuming a Poisson distribution, the 95 per cent confidence limits would be 0.62 to 8.77.

The incidence of SIDS in Denmark is about 0.1 per cent. The incidence of "near-miss" SIDS is unknown, but according to clinical experience, it is probably similar.

The mothers of the three children had uncomplicated pregnancies and deliveries. There was no disposition to febrile convulsion or epilepsy and no recurrence of paroxysmal morbidity. The child in Case 2 was resuscitated by two professional nurses. Since convulsion or excitation was not observed, febrile convulsions were unlikely, although her temperature on arrival at the hospital was 39.5°C.

Lead is a neurotoxic agent that passes the blood-brain and placental barriers. The developing nervous system is far more sensitive to lead than the adult nervous system. The toxic effect of lead on the respiratory center and the possible contribution of lead exposure to the occurrence of SIDS therefore requires thorough investigation.

TROELS LYNGBY, M.D.  Institute of Psychiatric Dermatology

OLE NOERBY HANSEN, M.PSYC.  Institute of Psychology

Aarhus, DK-8000, Denmark

LILIAN VANGBERT, M.D.  PHILIPPE GRANDJEAN, M.D., PH.D.

Odense, DK-5000, Denmark

In 1983-1984, first-grade children in the municipality of Aarhus, Denmark, were screened for lead absorption by measurement of the lead concentration in the secondary dentin of shed deciduous teeth. The screened cohort of 1302 children constituted 54 per cent of the eligible population. Children with the upper 8 per cent of tooth lead concentrations were selected and matched with children with the lowest concentrations, according to parental social group, sex, and school district.

A pedestrian who was blind to the lead data interviewed the parents about morbidity in the children, the medical background, and the possible sources of lead.

From interviews with 101 families of children with high levels of lead and 99 families of those with low levels, three cases of “near-miss” SIDS were found; they all belonged to the high-level group (Table 1). Assuming a Poisson distribution, the 95 per cent confidence limits would be 0.62 to 8.77.

The incidence of SIDS in Denmark is about 0.1 per cent. The incidence of “near-miss” SIDS is unknown, but according to clinical experience, it is probably similar.

The mothers of the three children had uncomplicated pregnancies and deliveries. There was no disposition to febrile convulsion or epilepsy and no recurrence of paroxysmal morbidity. The child in Case 2 was resuscitated by two professional nurses. Since convulsion or excitement was not observed, febrile convulsions were unlikely, although her temperature on arrival at the hospital was 39.5°C.

Lead is a neurotoxic agent that passes the blood-brain and placental barriers. The developing nervous system is far more sensitive to lead than the adult nervous system. The toxic effect of lead on the respiratory center and the possible contribution of lead exposure to the occurrence of SIDS therefore requires thorough investigation.